REMARKS

Claims 68-83 are pending. The claims are drawn to methods of alleviating a symptom of dry eye syndrome by administering a composition containing a carotenoid and a polyphenol and co-administering an omega-3 fatty acid. The remaining issues of patentability under 35 U.S.C 112, first paragraph, are discussed below.

The first issue relates to the nexus between dry eye syndrome, the many symptoms associated with dry eye, and inflammation. The Examiner acknowledges that dry eye is a well known disorder and states the following:

> However, the rejection was given to the phrase "a symptom of dry eye". Applicant in his remarks argues that dry eye is associated with many symptoms, which include itching, burning irritation, redness, blurred vision that improves with blinking, excessive tearing, increased discomfort after periods of reading, watching TV or working on a computer. The arguments have been noted. It is the examiner's position that the instant specification does not provide adequate description for using the claimed compounds or the combination of compounds for treating increased discomfort after periods of reading or watching TV, irritation, burning, itching, which can be caused by different sources different than dry eye.

Dry eye syndrome and its associated symptoms are known to be the result of inflammation (see Background of the Invention, page 1, lines 10-13, of the specification). The list of symptoms (e.g., itching, burning irritation, redness, etc.) were disclosed to be the manifestation of ocular tissue inflammation (page 2, lines 6-21, of the specification.) In fact, underlying mechanism of dry eye is acknowledged by the medical community to be inflammation. In a report entitiled "Management of Dry Eye Disease", the author states:

> Although a rtificial tears can improve DED [Dry Eye Disease] symptoms and objective findings, there is no evidence that they can resolve the inflammation that accompanies DED. Therefore, anti-inflammatory therapy may be indicated, including....
>
> *Topical corticosteroids.....*
> *Oral tetracyclines....*
> *Topical cyclosporine.*

(see page S98, middle of column 2, of Lemp, M., 2008, Am. J. of Managed Care 14:S88-S101; Exhibit A). Thus, the source of the symptoms of dry eye is recognized to be inflammation, and as disclosed in the specification (page 2, lines 27-30, of the specification), the invention features an anti-inflammatory composition, which is associated with reduced adverse side effects compared to conventional anti-inflammatory drugs (such corticosteroids, tetracyclines, and cyclosporine).

The second issue relates to the correlation between the structure and function of carotenoids, polyphenols, and omega-3 fatty acids as anti-inflammatory agents. Regarding this point, the Examiner states:

> Applicant's arguments regarding the lack of adequate written description regarding the terms "carotenoids", "polyphenol" and "omega-3 fatty acids" have been noted. Applicant in his remarks argues that the specification teaches a representative number of species by chemical name, formula, and function. It is the examiner's position that applicant has failed to establish a correlation between structure and function of group of compounds claimed. It is not clear that whether the function of treating dry eye is as a result of being a carotenoid, a polyphenol, or an omega-3 fatty acid or something else. It is also not clear whether the compounds having the structure of polyphenols, a carotenoid or an omega-3 fatty acids or the comounds discovered in the future with such structures are capable of treating dry eye.

Carotenoids and polyphenols lead to a reduction in inflammation and the symptoms of inflammation because of their anti-oxidant properties, and omega fatty acids are known as anti-inflammatory agents due to their effect on pro-inflammatory mediators such as prostaglandin. Carotenoids, such as astaxanthin, exhibit strong antioxidant properties and confer protection against lipid peroxidation and oxidative damage of cell membranes, cells, and tissues (page 6, lines 11-27, of the specification). Given that reactive oxygen species (ROS) activate pathways leading to increased expression and elevated production of proinflammatory mediators, the antioxidant properties of carotenoids impact the inflammatory process (Pashkow et al., 2008, Am. J. of Cardiol. 101 (10A): 58D-68D; Exhibit B). Moreover, carotenoids in combination with other agents lead to enhanced protection from inflammation (Fuller et al., 2006, J. of Cosmetic Derm. 5:30-38; Exhibit C). Polyphenolic compounds, such as curcuma longa root powder, green tea, grape extract, bilberry extract, quercetin, hops PE, blueberry powder,

tart cherry powder, or citrus bioflavonoids, are also established anti-oxidants (Rice-Evans et al., 1996, Free Radical Biology & Medicine 20:933-956; Exhibit D). As a result, this polyphenol class of compounds, e.g., green tea polyphenols, reduces inflammation (see, e.g., Tipoe et al., 2007, Cardiovascular &Haematological Disorders - Drug Targets 7:135-144; Exhibit E). Omega-3 fatty acids inhibit pro-infammatory mediators, such as prostaglandin (page 13, lines 11-13, of the specification). The role of omega-3 fatty acids in reducing inflammation is well established in the art (see, e.g., Simopoulos, A., 2002, J. Am. College of Nutrition 21:495-505; Exhibit F).

Applicants have established both the correlation between dry eye and inflammation as well as the correlation between structure and function of the key classes of compounds (carotenoids, polyphenols, and omega-3 fatty acids) as anti-inflammatory agents in the claimed methods. Applicants have cited portions of the originally-filed specification as well as provided copies of scientific journal articles as evidence of the role of inflammation in dry eye syndrome (and its symptoms) and as evidence of the anti-inflammatory activity of the classes of compounds required by the claims. In view of the disclosure provided in the specification and further supported by the attached publications, Applicants respectfully request withdrawal of this rejection.

CONCLUSION

Applicants believe that the application and claims are in condition for allowance. The Examiner is invited to contact the undersigned at the number or email listed below should she believe that there are any remaining issues that could be more easily resolved by personal or telephonic interview.

With a three-month extension of time, these documents are due on or before October 2, 2009. Applicants submit herewith a Petition for a Three-Month Extension of Time, together with an electronic payment in the amount of $555.00. The Commissioner is hereby authorized to charge any additional fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 21534-002CIP.

Respectfully submitted,

/Ingrid A. Beattie/

Ingrid A. Beattie, Reg. No. 42,306
Attorney for Applicants
c/o MINTZ, LEVIN
One Financial Center
Boston, Massachusetts 02111
IABeattie@mintz.com
Tel: (617) 542-6000
Fax: (617) 542-2241
Customer No. 30623

Dated: October 2, 2009

ACTIVE 4726870v.1